REMARKS

Upon entry of the present amendments, claims 1, 2, 4-8 and 11 are pending in the present application. Claims 2 and 11 have been amended. Support for the amendment to claim 2 can be found at page 230, lines 16-19 of the substitute specification. Claim 3 has been canceled, without prejudice. Applicants reserve the right to pursue the subject matter of this claim in a later application. No new matter has been added by the present amendments.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner has rejected claims 2, 3 and 11 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. *See*, Office Action at pages 2-4. Claim 3 has been cancelled. The rejection is traversed to the extent it applies to the claims 2 and 11 as amended herein.

The Examiner has rejected claim 2 stating that the term "stringent conditions" is confusing because it is a relative term. *See*, Office Action at pages 2-3. Applicants have amended claim 2 to recite specific high salt buffer, stringent, hybridization conditions "6X SSC at 65 °C".

The Examiner has also rejected claim 11 stating that claim 11 is indefinite because it depends from claim 3 and the nucleic acid of claim 3 requires the nucleic acid of claim 1 from which it depends to contain variations, which would be impossible. *See*, Office Action at page 4. Applicants have amended claim 11 to properly depend from claim 1.

Applicants submit that any person skilled in the art would be able to make and use the invention commensurate in scope with the claims 2 and 11, as amended herein, and therefore request withdrawal of the present rejection.

REJECTIONS UNDER 35 U.S.C. § 101

Claims 1-8 and 11 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. It is the Examiner's position that the asserted specific utilities for the claimed invention are simply

starting points for further research and investigation into potential practical uses of the claimed nucleic acids. Claim 3 has been cancelled. The rejection is traversed to the extent it applies to the remaining claims as amended herein.

Pending claims 1, 2, 4-8, and 11 are directed to nucleic acid molecules comprising SEQ ID NO:224, complements thereof, polypeptides encoded thereby, and compositions and methods containing such nucleic acid or polypeptide molecules. The specification discloses that SEQ ID NO:224 is homologous to known ORX family members (*See*, substitute specification page 215, line 41 to page 222, line 14) and contains the characteristic features of ORX family members including both a ORX ligand binding domain, and a heptahelical transmembrane domain within its overall sequence (*See,* substitute specification at page 216, line 16 - line 23). The presence of these domains within the overall sequence of SEQ ID NO:224 demonstrates that SEQ ID NO:224 is a novel member of the ORX family. Accordingly, one skilled in the art would recognize that the disclosed sequence of the polypeptide of the present invention, which contains these consensus domains, can be expected to function as a member of the ORX family.

The Utility Examination Guidelines further state that "when a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein." *See*, Fed. Reg., Vol. 66. No. 4, January 5, 2001, p. 1096). Applicants submit that the ORX protein family members share a specific, substantial, and credible utility and are sufficiently conserved, thereby imputing the same utility to a novel member of their protein class, such as proteins encoded by SEQ ID NO:224.

The Examiner has stated that there is no single substantial utility that is commonly shared among members of the ORX protein family. *See*, Office Action at page 4. Applicants submit that their action in the recognition and distinction of odors and involvement in cellular proliferation and differentiation represent substantial utilities commonly shared among members of the ORX protein family. Thus, SEQ ID NO:224 has a substantial utility in diagnosing, preventing and treating various diseases and disorders attributed to altered or aberrant function of ORX family members, as well as, differentiating between normal tissues and abnormal tissues linked to various diseases and disorders including, but not limited to, neurodegenerative, cell proliferative, angiogenic, hematopoietic, immunological, inflammatory, and tumor-related

disorders and/or pathologies as disclosed throughout the specification (*See*, substitute specification at page 281, lines 20-27). Therefore, Applicants assert that the polypeptide of SEQ ID NO:224, as a novel member of this family, has an art recognized specific, substantial, and credible utility. This conclusion is consistent with the Utility Examination Guidelines, which point out that the closest prior art applied in the course of prosecuting the application will demonstrate a well-established utility. *See, e.g.*, Fed. Reg., Vol. 66. No. 4, January 5, 2001, p. 1097. Here, the Examiner has asserted numerous references regarding the ORX superfamily as prior art against the claimed invention. Thus, the Examiner's maintenance of the utility rejection in view of the rejections under § 102 and § 103 is inconsistent.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-18 and 11 are rejected under 35 U.S.C. § 112, first paragraph for alleging that since the invention is not supported by either a specific or substantial asserted utility, one skilled in the art would not know how to use the claimed invention. Claim 3 has been cancelled. The rejection is traversed to the extent it applies to the remaining claims as amended herein.

For the reasons set forth above, Applicants submit that the claimed invention has a specific and substantial or well-established utility. Therefore, this rejection is now moot and should be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 103

Claims 1-8 are rejected under 35 U.S.C. 103(a) as obvious over Freitag et al., Neuron, 15(1383-1392) 1995 ("Freitag"). The Examiner states that Freitag teaches the amplification of genomic DNA using primers OR3.1-OR7.1 and therefore the claimed polynucleotides are not patentably distinct from those disclosed by Freitag. Further, the Examiner states that Applicants have admitted in Paper 10, page 2, that all derivatives of the ORX superfamily of nucleic acids and proteins, i.e., those obtained by using PCR consensus ORX primer pairs OR5B-OR3B and OR3.1-OR7.1, are not individually distinct and independent. Claim 3 has been cancelled. The rejection is traversed to the extent it applies to the remaining claims as amended herein.

It is well recognized under U.S. law, that any rejection of a claim for obviousness over a prior art reference must establish that: (1) the prior art reference produces the claimed invention; and (2) the prior art contains a suggestion or motivation to modify the prior art reference in such a way as to achieve the claimed invention. *In re Vaeck*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Pending claims 1, 2 and 4-8 are directed to nucleic acid molecules comprising SEQ ID NO:224, complements thereof, polypeptides encoded thereby, and compositions containing such nucleic acid molecules.

Freitag generally teaches the use of primers (including among others, OR3.1-OR7.1) for PCR using genomic DNA from *Xenopus laevis* as template in order to amplify a set of OR-related sequences. *See*, Freitag, Column 1, page 1384. Freitag discloses that of all the genes amplified only 9 *Xenopus laevis* sequences were in fact transcribed and subjected to sequence analysis. *See*, Freitag, Column 1, page 1384 – Column 1, page 1384 and Figure 4. Freitag does not teach or suggest the human nucleic acid sequence of SEQ ID NO:224, a complement thereof or a polypeptide encoded thereby. Thus, Freitag does not produce the claimed invention nor does Freitag contain a suggestion or motivation to modify its teachings to reach the claimed invention.

Although Applicants have previously stated that one of ordinary skill in the art would not be motivated to modify the teachings of Freitag to reach the present invention, as Freitag teaches only a few OR-related sequences from Xenopus laevis which are distinct from the mammalian (*e.g.* human) ORX genes claimed in the present invention, the Examiner states that Freitag teaches that the comparisons between frog receptors and corresponding mammalian receptors (particularly human) is important and would shed further light on the structure/function relationship involved in ligand binding. *See*, Office Action at page 6. While the comparison of receptors may be useful as disclosed in Freitag, the reason the comparison would be useful is due to the limited homology between species. Specifically, Freitag teaches that while frog receptors share 20-98% homology with one another, they exhibit 20-50% homology with representative rat sequences and 20-35% homology with fish sequences. Therefore, Applicants submit that Freitag along with not teaching or suggesting the human nucleic acid sequence of SEQ ID NO:224, a complement thereof or a polypeptide encoded thereby, also teaches away from the present invention because of the relatedness of these sequences between species.

Finally, the Examiner asserts that Applicants have admitted that the instantly claimed polynucleotides are not patentably distinct from those disclosed by Freitag as the claimed sequences and the sequences of Freitag were obtained using PCR primers OR3.1-OR7.1. Applicants submit that the Examiner has misconstrued these remarks and taken them out of context as these remarks were submitted in Response to the March 5, 2002 Restriction Requirement/Election of Species. Specifically, Applicants stated that **sequences of the present invention** (SEQ ID NOs 1-431) are derivatives of the ORX superfamily of nucleotides and proteins and that the nucleotides show high homology (>80%) and **as a result of this homology**, the ORX genes disclosed in the present patent application are not patentably distinct. (Emphasis Added). Applicants have made no assertion that the sequences of the present invention are not patentably distinct with respect to ORX nucleic acids or proteins in generally or specifically to the sequences disclosed in Freitag.

For the foregoing reasons, Applicants submit that Freitag does not teach or suggest the limitations of the claimed invention and pending claims 1, 2 and 4-8, as amended herein are patentably distinct and not obvious in view of the polynucleotides and polypeptides of Freitag. Applicants respectfully request this rejection be withdrawn.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as obvious over Ben-Arie et al., Human Molecular Genetics 3(2)229-235, 1994 ("Ben-Arie"). The Examiner states that Ben-Arie teaches the amplification of genomic DNA using primers OR5B-OR3B and therefore the claimed polynucleotides are not patentably distinct from those disclosed by Ben-Arie. Further, the Examiner states that Applicants have admitted in Paper 10, page 2, that all derivatives of the ORX superfamily of nucleic acids and proteins, i.e., those obtained by using PCR consensus ORX primer pairs OR5B-OR3B and OR3.1-OR7.1, are not individually distinct and independent. Claim 3 has been cancelled. The rejection is traversed to the extent it applies to the remaining claims as amended herein.

Ben-Arie teaches the cloning of 16 human olfactory receptor (OR) genes and the great sequence variability between those OR genes. Ben-Arie does not teach or suggest the human nucleic acid sequence of SEQ ID NO:224, a complement thereof or a polypeptide encoded thereby. Thus, Ben-Arie does not produce the claimed invention.

Moreover, Applicants submit that Ben-Arie teaches away from the nucleic acid molecule of SEQ ID NO:224 or a complement thereof or a polypeptide encoded thereby when it teaches that the cloned OR sequences display as much sequence variability as any randomly selected group of ORs. Thus, Ben-Arie does not produce the claimed invention nor does Ben-Arie contain a suggestion or motivation to modify its teachings to reach the claimed invention.

Finally, the Examiner asserts that Applicants have admitted that the instantly claimed polynucleotides are not patentably distinct from those disclosed by Ben-Arie as the claimed sequences and the sequences of Ben-Arie were obtained using PCR primers OR5B-OR3B. As discussed *supra*, Applicants have made no assertion that the sequences of the present invention are not patentably distinct with respect to ORX nucleic acids or proteins in generally or specifically to the sequences disclosed in Ben-Arie.

For the foregoing reasons, Applicants submit that Ben-Arie does not teach or suggest the limitations of the claimed invention and pending claims 1, 2 and 4-8, as amended herein, are patentably distinct and not obvious in view of the polynucleotides and polypeptides of Ben-Arie. Applicants respectfully request this rejection be withdrawn.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Freitag or Ben-Arie, in view of Kiefer et al., Biochemistry 1996, 35:16077-16084 ("Kiefer"). The Examiner states that the encoded receptor polypeptides taught by either Freitag or Ben-Arie could be produced using the method taught by Kiefer. Applicants traverse.

Applicants have amended claim 11 to indirectly depend from claim 1. Kiefer teaches the expression and purification of an olfactory receptor (OR5). As discussed *supra*, Freitag or Ben-Arie do not teach or suggest the human nucleic acid sequence of SEQ ID NO:224, a complement thereof or a polypeptide encoded thereby. Kiefer does not cure the deficiencies of Freitag or Ben-Arie as it also does not teach or suggest the human nucleic acid sequence of SEQ ID NO:224, a complement thereof or a polypeptide encoded thereby. Applicants submit that, while Kiefer teaches the expression of the O5 olfactory receptor, Kiefer in combination with the teachings of Freitag or Ben-Arie, does not teach or suggest expression of the human nucleic acid sequence of SEQ ID NO:224 or its complement.

Thus, Freitag or Ben-Arie in view of Kiefer do not teach or suggest all the limitations of the claimed invention. Accordingly, Applicants assert that claim 11, as amended herein, which depends from amended claim 1, is not anticipated by Freitag or Ben-Arie in view of Kiefer. Therefore, this rejection of these claims should be withdrawn.

For the foregoing reasons, Applicants submit that Freitag or Ben-Arie in view of Kiefer does not teach or suggest the limitations of the claimed invention and pending claim 11, as amended herein, is patentably distinct and not obvious in view of Freitag or Ben-Arie in view of Kiefer. Applicants respectfully request this rejection be withdrawn.

CLAIM OBJECTIONS

The Examiner has objected to claims 3 and 11 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of the previous claim. Specifically, the Examiner contends that claims 3 and 11 appear broader than parent claim 1, i.e. they claim the nucleic acid of claim 1 yet this nucleic acid can, at the same time, be different than that of claim 1.

Applicants have cancelled claim 3 and have amended claim 11 to properly depend from claim 1 and properly limit the subject matter of claim 1. Applicants request withdrawal of the present objection.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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